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Applicant(s) Levi, et al. Examiner: Unassigned  
Serial No.: 10/076,204 Group Art Unit: 1614  
Confirmation No: 8595 Docket: 955-16  
Filed: February 13, 2002 Dated: May 13, 2002  
For: METHOD AND  
COMPOSITION FOR  
REDUCING CARDIAC  
DYSFUNCTIONS WITH A  
SELECTIVE HISTAMINE  
H3 RECEPTOR AGONIST

Commissioner for Patents  
Washington, DC 20231

*I hereby certify this correspondence is being deposited with the United States Postal Service as first class mail, postpaid in an envelope, addressed to:*  
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*on May 13, 2002*

*Dated: 5/13/02*

**INFORMATION DISCLOSURE STATEMENT**

Sir:

In order to fulfill the requirements of candor and good faith set forth in 37 C.F.R. §1.56, Applicants submit herewith the following Information Disclosure Statement in accordance with the provisions of 37 C.F.R. §1.97 and §1.98.

**FOREIGN PATENT DOCUMENTS**

<b><u>COUNTRY</u></b>	<b><u>PUBLICATION NO.</u></b>	<b><u>PUBLICATION DATE</u></b>
PCT	WO 00/20011	April 13, 2000

### **NON-PATENT PUBLICATIONS**

1. B Malinowska, et al., "Histamine H<sub>3</sub> Receptors - General Characterization and Their Function in the Cardiovascular System", *Journal of Physiology and Pharmacology*, 1998. 49(2):191-211.
2. H. van der Goot, et al., "Isothiourea Analogues of Histamine as Potent Agonists or Antagonists of the Histamine H<sub>3</sub>-Receptor" *Eur. J. Med. Chem.* 1992. 27: 511-517.
3. Iwan J.P. De Esch, et al., "Characterization of the Binding Site of the Histamine H<sub>3</sub> Receptor. 1. Various Approaches to the Synthesis of 2-(1H-Imidazol-4-yl) cyclopropylamine and Histaminergic Activity of (1R,2R)- and (1S,2S)-2-(1H-Imidazol-4-yl)-cyclopropylamine", *Journal of Medicinal Chemistry*, 1999. 42(7): 1115-1122.
4. Christina J. Mackins, et al., "Therapeutic Potential of H<sub>3</sub>-receptor Agonists in Myocardial Infarction", *Exp. Opin. Invest Drugs* 2000. 9(11): 2537-2542.
5. Catherine Mazenot, et al., "Histamine H<sub>3</sub>-receptor Stimulation is Unable to Modulate Noradrenaline Release by the Isolated Rat Heart During Ischaemia-Reperfusion", *Fundam. Clin. Pharmacol.* 1999. 13(4): 455-60.
6. Catherine Mazenot, et al., "In vivo Demonstration of H<sub>3</sub>-histaminergic Inhibition of Cardiac Sympathetic Stimulation by R- $\alpha$ -methyl-histamine and its Prodrug BP 2.94 in the Dog", *British Journal of Pharmacology* 1999. 126: 264-268.

7. Pierre Theroux, M.D., "Myocardial Cell Protection. A Challenging Time for Action and Challenging Time of Clinical Research", *Circulation* 2000. 101:2874-2876.

8. Hans-Jurgen Rupprecht, M.D., et al., "Cardioprotective Effects of the  $\text{Na}^+/\text{H}^+$  Exchange Inhibitor Cariporide in Patients with Acute Anterior Myocardial Infarction Undergoing Direct PTCA", *Circulation* 2000. 101:2902-2908.

9. Morris Karmazyn, et al., "The Myocardial  $\text{Na}^+/\text{H}^+$  Exchange. Structure, Regulation and Its Role in Heart Disease", *Circulation Research* 1999. 85:777-786.

10. Eiichiro Hatta, et al., "Activation of Histamine  $\text{H}_3$  Receptors Inhibits Carrier-Mediated Norepinephrine Release in a Human Model of Protracted Myocardial Ischemia", *Journal of Pharmacology and Experimental Therapeutics* 1997. 283:494-500.

11. Randi B. Silver, et al., "Coupling of Histamine  $\text{H}_3$  Receptors to Neuronal  $\text{Na}^+/\text{H}^+$  Exchange: A Protective Mechanism in Myocardial Ischemia", *PNAS Early Edition* 2001. 1-5.

12. Rob Leurs, et al., "Therapeutic Potential of Histamine  $\text{H}_3$  Receptor Agonists and Antagonists", *Trends in Pharmacological Sciences* 1998. 19:177-183.

13. P.K. Rangachari, "The Fate of Released Histamine: Reception, Response and Termination", *Yale Journal of Biology and Medicine* 1998. 71:173-182.

14. Randi B. Silver, et al., "Coupling of Histamine H<sub>3</sub> receptors to Neuronal Na<sup>+</sup>/H<sup>+</sup> Exchange: A Novel Protective Mechanism in Myocardial Ischemia", *PNAS* 2001. 98(5):2855-2859.

15. Michiaki Imamura, et al., "Activation of Histamine H<sub>3</sub>-Receptors Inhibits Carrier-Mediated Norepinephrine Release During Protracted Myocardial Ischemia", *Circ. Res.* 1996. 78:475-481.

16. Roberto Levi, et al., "Histamine H<sub>3</sub>-Receptors: A New Frontier in Myocardial Ischemia", *The Journal of Pharmacology and Experimental Therapeutics* 2000. 292:825-830.

17. H.D. Holtje, et al., "Molecular Modelling Studies on Histamine H<sub>2</sub>- and H<sub>3</sub>- Receptor Agonists", [www.pharm.uni-duesseldorf.de/forschung/mitarbeiter/sippl/Maastricht.pdf](http://www.pharm.uni-duesseldorf.de/forschung/mitarbeiter/sippl/Maastricht.pdf). 1-12.

18. Patrizio Blandina, "The Role of Interactions Between Histaminergic and Cholinergic Systems in Learning and Memory", [www.mcmaster.ca/inabis98/huston/blandina0227/two.html](http://www.mcmaster.ca/inabis98/huston/blandina0227/two.html).

19. Rob Leurs, et al., "Histamine Receptors", *Tocris Cookson*. [www.biotrend.com/pdf/histamine.pdf](http://www.biotrend.com/pdf/histamine.pdf). 1-6.

The above-referenced documents are listed on PTO Form 1449. We have enclosed the cited documents to facilitate reference to them.

The Examiner is respectfully requested to consider these publications in their entirety, and to indicate that he or she has done so by initializing the enclosed form PTO-1449.

Applicants are not aware of any other references to be identified at this time. If the Examiner has any questions or comments relating to the present application, he or she is respectfully invited to contact Applicants' agent at the telephone number set forth below.

Respectfully submitted,

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